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Original Research

Relationship of lactate and lactate clearance with 28-day mortality in patients with acute renal injury in the emergency department

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Abstract

Aim : Acute kidney injury is frequently diagnosed in emergency departments; AKI should be included in the preliminary diagnosis in a wide range of symptoms, from loss of appetite, nausea, vomiting, which can be considered as a mild illness, to uremic encephalopathy, which can be a reason for loss of consciousness at hospital admission. The aim of our study is to show whether lactate and lactate clearance have an effect on 28-day mortality in these patients.

Material and Methods: In our study, the data of 600 patients who applied to the emergency department between 10.10.2019 and 10.06.2020 and were decided on dialysis treatment were examined prospectively. One hundred fifteen patients who met the inclusion criteria were included in the study. Age, gender, chronic diseases, laboratory findings, 28-day mortality status of the patients were recorded.

Results: In our study, in which 115 patients were evaluated, 51 patients (44.34%) deceased. In our study, when ROC analysis of lactate values was performed in patients who had a mortality in 28 days, it was predicted that 80.4% would have no mortality in 28 days for lactate values below 1,215 lactate levels; there may be a mortality rate of 40.6% at levels ≥1,215.

Discussion: AKI is an important cause of mortality and morbidity for patients admitted to the emergency department. It has been shown in our study that lactate is especially effective in mortality. It was found that the lactate clearance value of the deceased patients (-54,77±156,66) was lower than the lactate clearance of the survivors. The lactate 2 value was measured after dialysis in deceased patients, therefore, tissue perfusion and damage weres higher, but there was no statistically significant difference in lactate clearance values between survivors and deceased patients.

Keywords

Acute Kidney Injury, Emergency Department, Lactate, Lactate Clearance, Mortality

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Introduction

Acute kidney injury (AKI) can be defined as the deterioration of the filtration and excretory function of the kidney within days/weeks. This causes the retention of nitrogen and other waste products that are cleared from the blood by the kidneys. AKI is not a stand-alone disease; It is a clinical diagnosis that results in a decrease in urine output and an increase in serum creatinine levels. The presence of renal parenchymal damage may not be present, as it is not due to a structural disorder alone [1.2]. AKI is frequently diagnosed in emergency departments; AKI should be included in the preliminary diagnosis in a wide range of symptoms, from loss of appetite, nausea, vomiting, which can be considered as a mild illness, to uremic encephalopathy, which can be a reason for loss of consciousness at hospital admission [3]. It is an important complication, sometimes exceeding 50% in hospitalized patients (10-15% of all hospitalizations) and patients treated in intensive care units [4,5]. Blood gas analysis is important in the diagnosis and treatment of patients diagnosed with AKI; The blood gas parameters guide the patient's response to treatment/immediate hemodialysis decision.

Lactate in the human body is produced by the breakdown of pyruvate by the enzyme lactate dehydrogenase. In the normal physiological state, the reaction does not affect the lactate level, as it accounts for only one-tenth of the total pyruvate metabolism. As a result, intracellular lactate begins to multiply and pass into the bloodstream. Lactate has a molecular weight of 90 Da; its molecular weight is similar to urea (60 Da) that allows to be removed by hemodialysis [6]. It is thought that the lactate level, measured at the follow-up of the patient is an indicator of organ dysfunction and mortality. However, a single measurement of lactate may be due to static variability. In order to be more clinically useful, it is necessary to define the relationship between lactate clearance (LC) and clinical outcome, which is a measure of the change in lactate levels during the treatment process [7]. A negative result indicates an increase in lactate value compared to the reference after 6 hours, while a positive result indicates a decrease in lactate [8.9].

The aim of our study is to show whether lactate and lactate clearance have an effect on 28-day mortality in these patients.

Material and Methods

Patients who applied to the Emergency Medicine Clinic between 10.10.2019 and 10.06.2020 were examined prospectively. Patients who were diagnosed with acute kidney injury and consulted by a nephrologist and who were given emergency hemodialysis treatment were included in the study. AKI was diagnosed when the patient's serum creatinine level increased at least 1.5 times or GFR decreased by at least 25% and/or urine output was less than 0.5 ml/kg/h or the patient was anuric. The presence of severe hyperkalemia, severe acidosis, drug intoxication, pulmonary edema, and uremic symptoms were accepted as an indication for emergency hemodialysis [10]. Patient flow diagram is shown in Figure 1. Demographic characteristics, chronic diseases, laboratory parameters, etiological cause of AKI, and 28-day mortality status of 115 patients who met the inclusion criteria of our study were recorded in accordance with the purpose of the study. Lactate clearance was calculated as a percentage of the value obtained by dividing the difference between the lactate value at the time of initial admission and the lactate value measured 6 hours after by the initial lactate value.

Lactate clearance: [Lactate 1 - Lactate 2 (Value measured after 6 hours) x 100] / Lactate 1

Statistical analysis

The Kolmogorov-Smirnov normality test was used for continuous variables in the study. The non-parametric Mann-Whitney-U test was used for the median comparisons of two independent groups whose normality assumption was not provided ($p<0.05$) as a result of the test. The Independent Samples-t test was used to compare the means of two groups in normally distributed data. For non-normally distributed data, the Kruskal-Wallis test was used to compare medians in multiple groups. The Chi-square test was applied for ratio comparisons of independent frequency data (on 2x2, 3x2, etc. tables). The analysis of factors affecting mortality in patients diagnosed with AKI undergoing hemodialysis was performed with Multiple Logistic Regression analysis. ROC analysis was performed for parameters that were found to be significant for mortality and the area under the curve was calculated. Specificity-sensitivity ratios were calculated for the levels determined for the parameters with significant results. The value, which was used for statistical significance was $p<0.05$.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

In our study, there was no significant difference in age, living or deceased, and gender distirubition as shown in Table 1.

According to 28-day mortality, neutrophil 1-2, neutrophil-lymphocyte ratio 1-2, urea 1-2, creatine 1-2, white blood cell, pH 1-2, lactate 1-2, HCO3 2, BE 2, K 2 values were statistically significantly different between pre- and post-hemodialysis examinations between alive and deceased patients, as shown in Table 2. There was no significant difference between lactate clearance values. The mean clearance values for survivors were -25.77±80.32; It was found as -54.77±156.66 p 0.471 for those who deceased. Table 3 shows the multiple logistic regression analysis performed with the data obtained when the values that affect each other are subtracted among those with the most significant p-value on 28-day mortality which were evaluated in Table 2. Accordingly, lactate and creatine 1 levels were found to be significant and effective in predicting 28-day mortality.

In the tests mentioned above, it was concluded that the

Table 1. Demographic data of the groups

		Alive	Deceased
Gender*	Male	n=31 (%59.6)	n=21 (%40.4)
	Female	n=33 (%52.4)	n=30 (%47.6)
Age**	Min	24	24
	Max	94	109
	Mean	75	75

Min: Minimum, Max: Maximum. * Chi-square test; p=0.506. ** Mann-Whitney-U test; IQR; p=0,101

Table 2. Age and biochemical parameters according to the presence of death within 28 days

	28 Days Mortality								p-value
	Alive				Deceased				
	Mean±SD	Median	Min	Max	Mean±SD	Median	Min	Max	
Creatinin -1 (mg/dL)	6,5±4	6,7	0,9	23,7	4,6±2,7	4,1	1,1	15,2	0,004
Creatinin -2 (mg/dL)	4,7±2,7	4,3	0,6	14	3,5±1,7	2,9	1	8,9	0,017
pH -1	7,270±0,10	7,28	6,98	7,5	7,21±0,16	7,22	6,86	7,67	0,027
pH -2	7,35± 0,08	7,37	7,1	7,5	7,21±,21	7,27	6,53	7,45	0
K -2 (mmol/L)	4±1	4	2	7	5±1	5	2	8	0,026
Lactate -1 (mmol/L)	1,8±1,5	1,3	0,2	10,5	3,7±3,5	2,5	0,2	15,8	0
Lactate -2 (mmol/L)	1,8±1,1	1,4	0,5	8	4,7±4,7	2,7	0,2	20	0
Lactate Clearance	-25,77±80,32	,17	-406,41	62,58	-54,77±156,66	-22,03	-869,39	82	0,471

*Mann Whitney-U test; IQR, Independent Samples-t test; %95 CI p<0,001, ** Independent Samples-t test; %95 CI p<0,001, SD=standard deviation, Min.=Minimum, max.=Maximum

Table 3. ROC analysis

Variable(s)	Area	Std. Error	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Lactate	0,7	0,05	0,603	0,798
Cut-off values for Lactate				
	Cut-off	Sensitivity	1-Specificity	
Lactate	1,215	0,804	0,594	
	1,335	0,765	0,5	
	1,84	0,608	0,313	
	2,3	0,529	0,203	

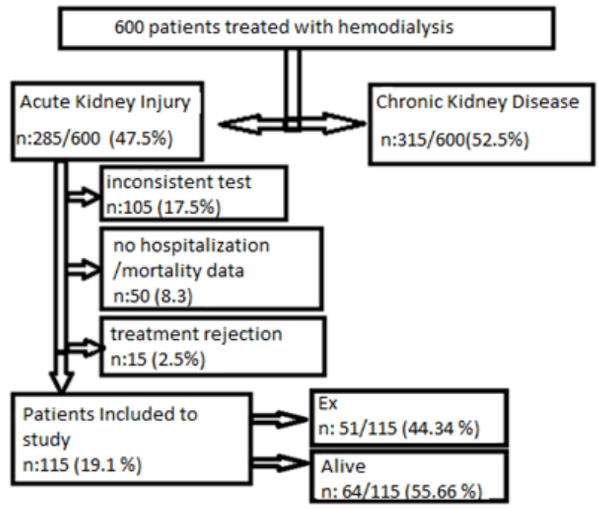

Figure 1. Patients Included in The Study

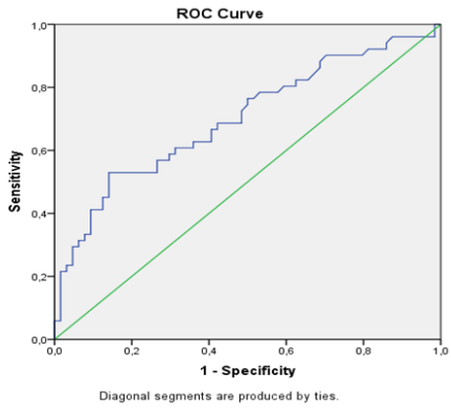

Figure 2. ROC analysis and area under the curve for lactate

relationship between lactate and 28-day mortality could be valuable. The area under the ROC curve (Figure 2) plotted on the

effect of lactate in predicting 28-day mortality, and the 95% confidence intervals are shown in Table 3. Here, the area under the curve (0.700) is statistically significant. Table 3 shows sensitivity and specificity rates for 28-day mortality estimation for some lactate levels. As an example, it can be interpreted as "80.4% will not die within 28 days at values below 1,215 lactate level, and 40.6% mortality may occur at levels ≥1,215 ".

Discussion

AKI has a clinical course that, if left untreated, is quite mortal [11]. When the data in 2016 were evaluated, it was determined that 66.4% of the patients were taken to emergency hemodialysis. The high rate can be interpreted in favor of asymptomatic patients not receiving treatment in the presence of underlying AKI. In case of emergency service admission, early diagnosis and rapid onset of etiological treatment are extremely important. In our study, the data of 115 patients who were diagnosed with AKI and received their first hemodialysis treatment at emergency service admission were evaluated. In our country, 57.52% of AKI and CKD patients who received the first hemodialysis treatment were male, 42.48% were female, and their mean age was between 45-64 (39.34%) years [12].

In our study, 45.2% of the patients were male and 54.8% were female, although this was not similar to the country in general, but there was no significant difference. However, the mean age of the patients included in our study was 73±14 years, which is higher than the national average. This may be due to the fact that patients over the age of 65 are diagnosed in the emergency room due to the disruption of their routine check-ups.

When GFR decreases, there is an increase in H+ and a decrease in HCO3-; the increase in unmeasured anions causes metabolic acidosis and the base deficit increases; this makes it a reliable parameter for us in monitoring acid production [13]. In our study, when the pH values were examined in terms of mortality before and after dialysis, a significant difference was found between the deceased and the alive patients, and it was found that the pH value was lower in the deceased group.

In the study conducted by Öztürk S. et al., high BUN and creatine and K+ levels were found to increase mortality [14]. In our study, although the mean values for urea and creatine decreased

after dialysis, there was a significant difference in mortality in Urea 1-2, Cre 1-2, K+ -2 parameters before and after dialysis. Although higher urea and K+ -2 values were detected in the mortal group, creatinine values showed a negative correlation. Here, it is thought that the creatinine value is lower in patients with a mortal course due to the high creatinine increase in postrenal aby cases and low postrenal aby mortality as the reason for the high creatinine level (postrenal AKI deceased K+-1 mean value 4,78, alive K+-1 mean value 10,5; deceased K+-2 mean value 3,47, alive K+-2 mean value 6,76).

Serum lactate is formed as a result of the glycolysis reaction due to tissue hypoxia and is considered an important biomarker for the evaluation of hemodynamic status in critically ill patients. It is metabolized in the liver and kidneys. Although lactate is a non-toxic molecule, the increase in concentration indicates significant changes in homeostasis and is therefore associated with increased mortality [15,16].

In studies based on the 'Surviving Sepsis Campaign' guideline on sepsis by Casserly et al. , high lactate levels were found to be highly correlated with mortality [17].

Similarly, in our study, a significant difference was found in the lactate 1-2 values before and after dialysis in patients who were alive and deceased; It is seen that the lactate values in the deceased group were high on arrival and after dialysis (alive patients' lactate-1 mean value: 1,8±1,5; Lactate -2: 1,8±1,1, in deceased patients, Lactate-1 mean value: . 3,7±3,5 ; Lactate-2: 4,7±4,7, p<0,05).

When the ROC analysis of the lactate values of the patients who had mortality in 28 days in our study was performed, it was predicted that there would be no mortality in 28 days at a rate of 80.4% in the values below 1.215 mg/dL. Here, the area under the curve (0.700) is statistically significant. Table 3 shows sensitivity and specificity rates for 28-day mortality estimation for some lactate levels. To give an example, it can be interpreted as "80.4% will not die within 28 days at lactate levels below 1,215, and 40.6% mortality may occur at levels ≥1,215 ".

An increase in lactate clearance may indicate resolution of global tissue hypoxia and is associated with a reduced mortality rate in patients with severe sepsis and septic shock [18]. Therefore, lactate clearance is used as a target in the resuscitation of sepsis [19].

Similarly, in our study, it was found that the lactate clearance value of the deceased patients (-54,77±156,66) was lower than the lactate clearance of the survivors (-25,77±80,32). We think that deterioration of kidney functions and an increase in lactate production due to etiology or septic condition occur as a decrease in lactate clearance. The finding obtained in our studyis that the lactate 2 value was measured after dialysis in deceased patients and therefore tissue perfusion and damage were higher, and there was no statistically significant difference in lactate clearance values between survivors and deceased patients. The lack of a significant difference here can be attributed to the low number of patients in the group, and further studies with a larger number of patients are needed.

In the study conducted by Passos R. et al., arrival lactate, lactate value at 4 and 24 hours after dialysis, and lactate clearance were evaluated; Lactate clearance of more than 10% was found to be associated with survival, and the 24th hour lactate value was found to be more prognostically significant. Lactate clearance, which was calculated using the 24th hour lactate value, was found to be associated with a decrease in mortality independent of other factors [20].

Limitations

The biggest limitation of our study is the small number of patients. Apart from this, the inability to differentiate patients according to etiology is another limitation. Failure to upload laboratory findings to the system due to device failure during the working process, the fact that patients who were transferred to another center after dialysis / hospitalized in the external service and intensive care unit could not be followed up in the post-emergency department period played a major role in limiting the number of patients. The importance of data archiving and proper recording of patient information in the system during patient follow-up is clear.

Conclusion

AKI is an important cause of mortality and morbidity for patients admitted to the emergency department. In the literature we searched during our study, very few studies have been found about the effect of lactate and lactate clearance on mortality in AKI in the emergency department. It has been shown in our study that lactate is especially effective on mortality. However, we think that there is a need to study lactate clearance in a larger number of patients.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content, including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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